SUPPLEMENTARY MATERIAL

Incidence and predictors of ocular complications in pediatric-onset uveitis: data from the AIDA Network Uveitis Registry

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Table S1. List of the Ethics Committees which approved the study conduction at the AIDA Network partner institutions.

AIDA Network partner center	Ethics Committee
Siena University Hospital, Siena, Italy	Ethics Committee of Siena University Hospital
Universidad del Rosario, Bogotá, Colombia	Comité de ética en investigación Universidad del Rosario (CEI-UR)
Bari University, Bari, Italy	Comitato Etico Interregionale dell'Azienda Policlinico di Bari
Cairo University, Giza, Egypt	Gazi University Faculty of Medicine Ethics Committee
Sapienza University of Rome, Rome, Italy	Ethics Committee of Sapienza University
S.S. Annunziata Hospital, Chieti, Italy	Comitato etico per la ricerca biomedica delle province di Chieti e di Pescara
Sapienza University of Rome, Polo Pontino, Latina, Italy	Comitato Etico Territoriale Lazio AREA 1
Vito Fazzi Hospital, Lecce, Italy	Comitato Etico della ASL di Lecce
University of Brescia, Brescia, Italy	Comitato Etico di Brescia, sezione ASST degli Spedali Civili di Brescia
Fatebenefratelli-Sacco Hospital, Milan, Italy	Ethics Committee of Milan Area 1
King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia	Alfaisal University Ethics Committee
University of Tripoli, Tripoli, Libya	Tripoli Children Hospital Ethics Commitee
Cruces University Hospital, University of the Basque Country, Barakaldo, Bizkaia, Spain	Comité ético de Investigación con medicamentos de Euskadi
National and Kapodistrian University of Athens, General University Hospital "Attikon", Athens, Greece	Ethics Committee of Laikon Hospital
University of Campania "Luigi Vanvitelli", Naples, Italy	Comitato Etico Università degli Studi della Campania "Luigi Vanvitelli"

University of Palermo, Palermo, Italy	Comitato Etico Palermo 2
University of Rome “Tor Vergata”, Rome, Italy	Comitato Etico territoriale Lazio area 2
Hacettepe University School of Medicine, Ankara, Turkey	Hacettepe University Non-interventional Clinical Researches Ethics Board, Sıhhiye
Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy	Ethics Committee of Milan Area 2
Gazi University Hospital, Ankara, Turkey	Gazi University Faculty of Medicine Ethics Committee
Prabha Eye Clinic and Research Centre and Vittala International Institute of Ophthalmology, Jayanagar, Bengaluru, Karnataka, India	Science for Health, Jnana Sanjeevani Diabetes Hospital and Medical centre campus Ethics Committee
Al-Azhar University, Assuit, Egypt	Al-Azhar University faculty of Medicine, Assiut Ethics committee
AOU "Policlinico-San Marco", Catania, Italy	Comitato Etico Catania 1
Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico	Ethics Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán
Ospedale San Paolo di Civitavecchia, Civitavecchia, Rome, Italy	Comitato Etico della ASL Roma 4
University of Ferrara, Ferrara, Italy	Comitato Etico dell’Area Vasta Emilia Centro
University of Messina, Messina, Italy	Comitato Etico di Messina
University of Sousse, Sousse, Tunisia	Farhat Hached Hospital Ethics Committee
La Paz University Hospital, Madrid, Spain	Comité de Ética de la Investigación de la Fundación Jiménez Díaz
Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India	Postgraduate Institute of Medical Education and Research Ethics Committee

Table S2. Therapeutic data of the study population. List of abbreviations: bDMARDs, biologic disease-modifying anti-rheumatic drugs; cDMARDs, conventional disease-modifying anti-rheumatic drugs; IL, interleukin; IQR, interquartile range; max, maximum value; min, minimum value; TNF, tumor necrosis factor; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs.

Drug or drug group	**Patients (%)**
cDMARDs (at least one)	226 (73.1)
– Methotrexate	189 (61.2)
– Cyclosporine A	27 (8.7)
– Azathioprine	25 (8.1)
– Mycophenolate Mofetil	10 (3.2)
– Other cDMARDs	16 (5.2)
bDMARDs or tsDMARDs (at least one)	153 (49.5)
– TNF inhibitors	150 (48.5)
– IL-6 inhibitors	11 (3.6)
– Other bDMARDs or tsDMARDs	8 (2.6)
Glucocorticoid monotherapy, drops	204 (66.0)
Glucocorticoid monotherapy, systemic	102 (33.0)
Glucocorticoid, regional	17 (5.5)
Intravitreal dexamethasone implant	2 (0.6)
Intravitreal injections (bevacizumab, ranibizumab)	3 (1.0)
Dilator or cycloplegic	161 (52.1)
Intervention	**Eyes (%)**
Surgery (any)	53 (9.9)
– Phacoemulsification	36 (6.8)
– Vitrectomy	16 (3.0)
– Laser Retinal Photocoagulation	8 (1.5)
– Other surgical interventions	5 (1.2)
Continuous variables	**Median (IQR) [min – max]**
Duration of glucocorticoid drops as monotherapy, months	3.0 (9.0) [0 – 48.0]
Systemic glucocorticoid therapy delay, months	4.0 (10.5) [0 – 204]
Duration of systemic glucocorticoid therapy, months	5.0 (10.0) [0 – 147.0]
DMARD therapy delay, months	6.0 (15.5) [0 – 564.0]
Duration of cDMARD therapy, months	22.0 (54.0) [1.0 – 348.0]
b/tsDMARD therapy delay, months	21.0 (54.0) [0 – 603.0]
Duration of b/tsDMARD therapy, months	24.0 (41.3) [1.0 – 825.0]

Table S3. Factors associated with the presence of any ocular complication of uveitis during the disease history. List of abbreviations: BCVA, best corrected visual acuity; bDMARDs, biologic disease-modifying anti-rheumatic drugs; cDMARDs, conventional disease-modifying anti-rheumatic drugs; HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis.

Factors		**Patients/eyes with at least one complication**	***p*-value**
Ethnic origin	Hispanic	35 (55.6%)	0.001
	Arab	30 (53.6%)	
	White	146 (37.3%)	
Uveitis anatomical classification	Panuveitis	76 (62.8%)	<0.001
	Intermediate	44 (50.0%)	
	Anterior	85 (29.3%)	
	Posterior	7 (29.2%)	
Systemic disease association	No	132 (48.2%)	<0.001
	Yes	81 (32.5%)	
Associated disease	Blau syndrome	9 (69.2%)	<0.001
	Vogt-Koyanagi-Harada syndrome	6 (75.0%)	
	HLA-B27 – related diseases	16 (69.6%)	
	JIA	54 (28.7%)	
	Others	3 (30.0%)	
	Behçet's disease	3 (15.8%)	
Duration of uveitis	Persistent	164 (48.2%)	<0.001
	Limited	15 (16.5%)	
Course of uveitis	Chronic	99 (59.6%)	<0.001
	Recurrent	65 (37.4%)	
	Acute	15 (16.5%)	
Therapeutic approach	bDMARDs	129 (48.5%)	<0.001
	cDMARDs	55 (33.9%)	
	No DMARDs	32 (29.9%)	
Surgery	Performed	48 (90.6%)	<0.001
	Not performed	168 (34.9%)	
Continuous variables		**Median (IQR)**	***p*-value**
Duration of topical glucocorticoid monotherapy (months)	Group with complications	6.0 (12.5)	<0.001
	Group without complications	3.0 (5.0)	

DMARD therapy delay (months)	Group with complications	7.0 (31.0)	0.03
	Group without complications	4.0 (10.0)	
Follow-up duration (months)	Group with complications	58.0 (114.0)	0.001
	Group without complications	41.0 (89.5)	
Final BCVA	Group with complications	1.00 (0.30)	<0.001
	Group without complications	1.00 (0.00)	

Table S4. Statistically significant associations emerging from univariate analysis of factors associated with the development of cataract. List of abbreviations: BCVA, best corrected visual acuity; bDMARDs, biologic disease-modifying anti-rheumatic drugs; cDMARDs, conventional disease-modifying anti-rheumatic drugs; HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis.

Factors		**Patients/eyes with cataract**	***p*-value**
Ethnic origin	Arab	18 (32.1%)	0.02
	Hispanic	14 (22.2%)	
	White	58 (14.8%)	
Uveitis anatomical classification	Panuveitis	33 (27.3%)	0.006
	Intermediate	13 (14.8%)	
	Anterior	41 (14.1%)	
	Posterior	2 (8.3%)	
Associated disease	Blau syndrome/sarcoidosis	6 (46.2%)	0.02
	HLA-B27 – related diseases	6 (26.1%)	
	JIA	25 (13.3%)	
	Behçet's disease	2 (10.5%)	
	others	1 (10.0%)	
	Vogt-Koyanagi-Harada syndrome	0 (0.0%)	
Duration of uveitis	Persistent	64 (18.8%)	0.03
	Limited	8 (8.8%)	
Course of uveitis	Chronic	41 (24.7%)	0.001
	Recurrent	23 (13.2%)	
	Acute	8 (8.8%)	
Therapeutic approach	bDMARDs	58 (21.8%)	0.02
	No DMARDs	15 (14.0%)	
	cDMARDs	19 (11.7%)	
Surgery	Performed	29 (54.7%)	<0.001
	Not performed	63 (13.1%)	
Continuous variables		**Median (IQR)**	***p*-value**
Age at uveitis onset	Group with cataract	7.8 (6.7)	0.04
	Group without cataract	7.9 (6.5)	
Duration of topical glucocorticoid monotherapy (months)	Group with cataract	6.0 (12.5)	0.001
	Group without cataract	3.0 (5.0)	
DMARD therapy delay (months)	Group with cataract	7.0 (31.0)	0.004
	Group without cataract	4.0 (10.0)	
	Group with cataract	60.5 (116.3)	<0.001

Follow-up duration (months)	Group without cataract	41.0 (88.8)	
Final BCVA	Group with cataract	1.00 (0.30)	<0.001
	Group without cataract	1.00 (0.00)	

Table S5. Statistically significant associations emerging from univariate analysis of factors associated with the development of posterior synechiae. List of abbreviations: BCVA, best corrected visual acuity; bDMARDs, biologic disease-modifying anti-rheumatic drugs; cDMARDs, conventional disease-modifying anti-rheumatic drugs; HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis.

Factors		**Patients/eyes with posterior synechiae**	***p*-value**
Ethnic origin	Arab	17 (30.4%)	<0.001
	Hispanic	13 (20.6%)	
	White	48 (12.3%)	
Type of inflammation	Granulomatous	19 (34.5%)	<0.001
	Non-granulomatous	52 (14.9%)	
Associated disease	Vogt-Koyanagi-Harada syndrome	4 (50.0%)	<0.001
	Blau syndrome/sarcoidosis	5 (38.5%)	
	HLA-B27 – related diseases	7 (30.4%)	
	JIA	22 (11.7%)	
	others	1 (8.3%)	
	Behçet's disease	0 (0.0%)	
Duration of uveitis	Persistent	70 (20.6%)	<0.001
	Limited	2 (2.2%)	
Course of uveitis	Chronic	47 (28.3%)	<0.001
	Recurrent	23 (13.2%)	
	Acute	2 (2.2%)	
Use of dilator or cycloplegic drugs	Yes	56 (20.1%)	0.02
	No	24 (12.0%)	
Therapeutic approach	bDMARDs	57 (21.4%)	<0.001
	cDMARDs	16 (9.9%)	
	No DMARDs	7 (6.5%)	
Surgery	Performed	61 (12.7%)	<0.001
	Not performed	19 (35.8%)	
Continuous variables		**Median (IQR)**	***p*-value**
Duration of topical glucocorticoid monotherapy (months)	Group with posterior synechiae	8.0 (19.0)	0.004
	Group without posterior synechiae	3.0 (7.0)	
DMARD therapy delay (months)	Group with posterior synechiae	7.0 (28.0)	0.01
	Group without posterior synechiae	6.0 (15.0)	
Final BCVA	Group with posterior synechiae	0.90 (0.30)	<0.001

	Group without posterior synechiae	1.00 (0.10)	

Table S6. Statistically significant associations emerging from univariate analysis of factors associated with the development of macular edema. List of abbreviations: HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis.

Factors		**Eyes/patients with macular edema**	***p*-value**
Associated disease	HLA-B27 – related diseases	7 (30.4%)	<0.001
	others	3 (25.0%)	
	JIA	6 (3.2%)	
	Vogt-Koyanagi-Harada syndrome	0 (0.0%)	
	Blau syndrome/sarcoidosis	0 (0.0%)	
	Behçet's disease	0 (0.0%)	
Association with a systemic disease	No	33 (12.0%)	0.01
	Yes	14 (5.6%)	
Uveitis anatomical classification	Intermediate	19 (21.6%)	<0.001
	Panuveitis	21 (17.4%)	
	Posterior	3 (12.5%)	
	Anterior	3 (1.0%)	
Continuous variables		**Median (IQR)**	***p*-value**
bDMARD therapy delay (months)	Group with macular edema	10.0 (26.3)	0.02
	Group without macular edema	23.5 (63.0)	

Table S7. Statistically significant associations emerging from univariate analysis of factors associated with the development of band keratopathy. List of abbreviations: BCVA, best corrected visual acuity; DMARDs, disease-modifying anti-rheumatic drugs.

Factors		**Eyes/patients with band keratopathy**	***p*-value**
Ethnic origin	Hispanic	10 (15.9%)	0.02
	White	24 (6.1%)	
	Arab	3 (5.4%)	
Uveitis anatomical classification	Anterior	36 (8.8%)	0.049
	Non anterior	3 (2.8%)	
Duration of uveitis	Persistent	29 (8.5%)	0.03
	Limited	1 (1.1%)	
Course of uveitis	Chronic	15 (9.0%)	0.04
	Recurrent	14 (8.0%)	
	Acute	1 (1.1%)	
Surgery	Performed	17 (32.1%)	<0.001
	Not performed	23 (4.7%)	
Continuous variables		**Median (IQR)**	***p*-value**
Age at uveitis onset	Group with band keratopathy	Median 4.5 (IQR 3.2)	<0.001
	Group without band keratopathy	Median 8.2 (IQR 7.1)	
DMARD therapy delay (months)	Group with band keratopathy	Median 16.0 (IQR 31.5)	0.04
	Group without band keratopathy	Median 6.0 (IQR 13.0)	
Follow-up duration (months)	Group with band keratopathy	Median 108.0 (IQR 99.5)	0.007
	Group without band keratopathy	Median 44.0 (IQR 91.0)	
Final BCVA	Group with band keratopathy	Median 1.00 (IQR 0.30)	0.04
	Group without band keratopathy	Median 1.00 (IQR 0.10)	

Table S8. Statistically significant associations emerging from univariate analysis of factors associated with the development of glaucoma/ocular hypertension. List of abbreviations: BCVA, best corrected visual acuity.

Factors		**Eyes/patients with glaucoma/ocular hypertension**	***p*-value**
Ethnic origin	Arab	11 (19.6%)	0.004
	Hispanic	7 (11.1%)	
	White	26 (6.7%)	
Uveitis anatomical classification	Panuveitis	17 (14.1%)	0.03
	Intermediate	10 (11.4%)	
	Anterior	17 (5.9%)	
	Posterior	1 (4.2%)	
Type of inflammation	Granulomatous	12 (21.8%)	0.002
	Non-granulomatous	29 (8.3%)	
Association with a systemic disease	Yes	14 (5.6%)	0.02
	No	31 (11.3%)	
Associated disease	Blau syndrome/sarcoidosis	3 (23.1%)	0.01
	Vogt-Koyanagi-Harada syndrome	2 (25.0%)	
	HLA-B27 – related diseases	2 (8.7%)	
	others	1 (8.3%)	
	JIA	8 (4.3%)	
	Behçet's disease	0 (0%)	
Onset	Insidious	30 (11.6%)	0.01
	Sudden	8 (4.7%)	
Duration of uveitis	Persistent	40 (11.8%)	0.004
	Limited	1 (1.1%)	
Course of uveitis	Chronic	28 (16.9%)	<0.001
	Recurrent	12 (6.9%)	
	Acute	1 (1.1%)	
Cataract surgery	Performed	11 (30.6%)	<0.001
	Not performed	34 (6.8%)	
Continuous variables		**Median (IQR)**	***p*-value**
Duration of topical glucocorticoid monotherapy (months)	Group with ocular hypertension	12.0 (14.0)	<0.001
	Group without ocular hypertension	3.0 (7.0)	
Final BCVA	Group with ocular hypertension	0.90 (0.20)	<0.001

	Group without ocular hypertension	1.00 (0.20)	